

# CLAIMS

What is claimed is:

1. A method for desorption and ionization of analytes, comprising the steps of:
  - a. preparing a sample comprising analytes in a medium having at least one component;
  - b. selecting a resonant vibrational mode of at least one component of the medium;
  - c. selecting a laser turned on to emit light substantially at the wavelength of the selected vibrational mode; and
  - d. irradiating the sample with the laser light to cause medium ablation and desorption and ionization of the analytes.
2. The method of claim 1, wherein the step of preparing a sample comprises a step of stabilizing the sample for compatibility with high-vacuum conditions.
3. The method of claim 2, wherein the stabilizing step comprises a step of freezing the sample at a sufficiently low temperature so that at least part of the sample has a phase transition.
4. The method of claim 3, wherein the freezing step comprises the steps of placing the sample in a sample support, and immersing the sample support in liquid nitrogen for a period of time so that any water within the sample changes to ice.
5. The method of claim 2, wherein the stabilizing step comprises a step of freezing the sample at a sufficiently low temperature so that at least part of the sample has an increase in viscosity and a decrease in vapor pressure.
6. The method of claim 1, wherein the step of preparing a sample comprises a step of

spatially separating the analytes within the medium by electrophoresis, and the step of irradiating the sample comprises a step of irradiating sequentially a plurality of positions within the sample, wherein at least two irradiated positions correspond to locations of the spatially separated analytes.

7. The method of claim 6, wherein each of the plurality of positions is irradiated by laser light delivered in pulses, each pulse having a duration of less than the relaxation time of the selected vibrational mode, wherein the pulses are separated in time by intervals, each interval having a duration of at least ten times the relaxation time of the selected vibrational mode.
8. The method of claim 6, wherein each of the plurality of positions is irradiated by laser light delivered in pulses, each pulse having a duration of less than a thermal relaxation time of the at least one component of the medium.
9. The method of claim 6, wherein each of the plurality of positions is irradiated by laser light delivered in pulses, each pulse having a duration of less than a mechanical relaxation time of the at least one component of the medium.
10. The method of claim 1, wherein the step of selecting a resonant vibrational mode comprises a step of locating the resonant vibrational mode from a Fourier-transform infrared absorption spectrum of the medium.
11. The method of claim 1, wherein the step of irradiating the sample with the laser light comprises a step of delivering the laser light in pulses, wherein the pulses are separated in time by intervals, each interval having a duration of at least ten times the relaxation time of the selected vibrational mode.
12. The method of claim 11, further comprising a step of moving the sample in a

relative motion back and forth to the laser light to form a rastering trace such that the desorption and ionization of the analytes occur substantially at a same region in space.

13. The method of claim 1, wherein the medium includes an electrophoresis medium.
14. The method of claim 13, wherein the electrophoresis medium comprises polyacrylamide.
15. The method of claim 1, wherein the step of preparing a sample comprises a step of stabilizing the sample for compatibility with atmospheric pressure conditions.
16. The method of claim 1, further comprising the steps of:
  - a. passing the ionized analytes through a mass spectrometer; and
  - b. obtaining a mass spectrum of the ionized analytes.
17. A system for desorption and ionization of analytes, comprising:
  - a. means for preparing a sample comprising analytes in a medium having at least one component;
  - b. means for selecting a resonant vibrational mode of at least one component of the medium;
  - c. means for tuning a laser to emit light substantially at the wavelength of the selected vibrational mode; and
  - d. means for irradiating the sample to cause medium ablation and desorption and ionization of the analytes.
18. The system of claim 17, wherein the preparing means includes means for freezing the sample at a sufficiently low temperature so that at least part of the sample has a phase transition.

19. The system of claim 17, wherein the preparing means includes means for freezing the sample at a sufficiently low temperature so that at least part of the sample has an increase in viscosity and a decrease in vapor pressure.
20. The system of claim 17, wherein the irradiating means includes means for delivering light in pulses, each pulse having a duration of less than the relaxation time of the selected vibrational mode, wherein the pulses are separated in time by intervals, each interval having a duration of at least ten times the relaxation time of the selected vibrational mode.
21. The system of claim 17, wherein the irradiating means includes means for delivering light in pulses, each pulse having a duration of less than a thermal relaxation time of the at least one component of the medium.
22. The system of claim 17, wherein the irradiating means includes means for delivering light in pulses, each pulse having a duration of less than a mechanical relaxation time of the at least one component of the medium.
23. A method for desorption and ionization of analytes, comprising the steps of:
  - a. preparing a sample having analytes and a polyacrylamide medium having at least one component;
  - b. selecting a resonant vibrational mode of at least one component of the medium;
  - c. selecting a laser tuned to emit light substantially at the wavelength of the selected vibrational mode; and
  - d. irradiating the sample with laser light to cause medium ablation and desorption and ionization of the analytes.
24. The method of claim 23, wherein the laser emits light at a wavelength greater than

4.5 micrometers and less than 10.0 micrometers.

25. The method of claim 23, wherein the laser emits light at a wavelength greater than 5.7 micrometers and less than 6.5 micrometers.
26. The method of claim 23, wherein the laser emits light at a wavelength greater than 6.7 micrometers and less than 7.3 micrometers.
27. The method of claim 23, wherein the laser emits light at a wavelength greater than 7.3 micrometers and less than 9.8 micrometers.
28. The method of claim 23, wherein the sample is irradiated by laser light delivered in pulses, each pulse having a duration of less than 5.0 picoseconds, wherein the pulses are separated in time by more than 100 picoseconds.
29. The method of claim 23, wherein the step of preparing a sample comprises a step of stabilizing the sample for compatibility with high-vacuum conditions.
30. The method of claim 29, wherein the stabilizing step comprises a step of freezing the sample at a sufficiently low temperature so that at least part of the sample has a phase transition.
31. The method of claim 30, wherein the freezing step comprises the steps of placing the sample in a sample support, and immersing the sample support in liquid nitrogen for a period of time so that any water within the sample changes to ice.
32. The method of claim 29, wherein the stabilizing step comprises a step of freezing the sample at a sufficiently low temperature so that at least part of the sample has an increase in viscosity and a decrease in vapor pressure.

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33. The method of claim 23, wherein the step of preparing a sample comprises a step of stabilizing the sample for compatibility with atmospheric pressure conditions.
34. The method of claim 23, wherein the step of preparing a sample comprises a step of spatially separating the analytes within the medium by electrophoresis, and the step of irradiating the sample comprises a step of irradiating sequentially a plurality of positions within the sample, wherein at least two irradiated positions correspond to locations of the spatially separated analytes.
35. The method of claim 34, wherein each of the plurality of positions is irradiated by laser light delivered in pulses, each pulse having a duration of less than the relaxation time of the selected vibrational mode, wherein the pulses are separated in time by intervals, each interval having a duration of at least ten times the relaxation time of the selected vibrational mode.
36. The method of claim 34, wherein each of the plurality of positions is irradiated by laser light delivered in pulses, each pulse having a duration of less than a thermal relaxation time of the at least one component of the medium.
37. The method of claim 34, wherein each of the plurality of positions is irradiated by laser light delivered in pulses, each pulse having a duration of less than a mechanical relaxation time of the at least one component of the medium.
38. The method of claim 23, wherein the step of selecting a resonant vibrational mode comprises a step of locating the resonant vibrational mode from a Fourier-transform infrared absorption spectrum of the polyacrylamide medium.
39. The method of claim 23, further comprising the steps of:
- a. passing the ionized analytes through a mass spectrometer; and

- b. obtaining a mass spectrum of the ionized analytes.
- 40. A system for desorption and ionization of analytes, comprising:
  - a. means for preparing a sample having analytes and a polyacrylamide medium having at least one component;
  - b. means for selecting a resonant vibrational mode of at least one component of the medium;
  - c. means for tuning a laser to emit light substantially at the wavelength of the selected vibrational mode; and
  - d. means for irradiating the sample with laser light to cause medium ablation and desorption and ionization of the analytes.
- 41. The system of claim 40, wherein the preparing means includes means for stabilizing the sample for compatibility with high-vacuum conditions.
- 42. The system of claim 40, wherein the irradiating means includes means for delivering light in pulses, each pulse having a duration of less than the relaxation time of the selected vibrational mode, wherein the pulses are separated in time by intervals, each interval having a duration of at least ten times the relaxation time of the selected vibrational mode.
- 43. The system of claim 40, wherein the irradiating means includes means for delivering light in pulses, each pulse having a duration of less than a thermal relaxation time of the at least one component of the medium.
- 44. The system of claim 40, wherein the irradiating means includes means for delivering light in pulses, each pulse having a duration of less than a mechanical relaxation time of the at least one component of the medium.

45. The system of claim 40, further comprising means for obtaining a mass spectrum of the ionized analytes.
46. A method for desorption and ionization of analytes, comprising the steps of:
  - a. preparing a sample having analytes in a medium including at least one component;
  - b. freezing the sample at a sufficiently low temperature so that at least part of the sample has an increase in viscosity and a decrease in vapor pressure; and
  - c. irradiating the frozen sample with short-pulse radiation to cause medium ablation and desorption and ionization of the analytes.
47. The method of claim 46, further comprising the steps of:
  - a. selecting a resonant vibrational mode of at least one component of the medium; and
  - b. selecting an energy source to emit short-pulse radiation substantially at the wavelength of the selected resonant vibrational mode.
48. The method of claim 47, wherein the energy source is a laser.
49. The method of claim 48, wherein the laser is a free electron laser.
50. The method of claim 49, wherein the free electron laser is tunable to generate short-pulse radiation.
51. The method of claim 48, wherein the laser is a solid state laser.
52. The method of claim 51, wherein the solid state laser is tunable to generate short-pulse radiation.

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53. The method of claim 48, wherein the laser is a gas laser.
54. The method of claim 48, wherein the laser is a metal vapor laser.
55. The method of claim 47, wherein the step of selecting a resonant vibrational mode comprises a step of locating the resonant vibrational mode from a Fourier-transform infrared absorption spectrum of the medium.
56. The method of claim 46, wherein the freezing step comprises the steps of placing the sample in a sample support, and immersing the sample support in liquid nitrogen for a period of time so that any water within the sample has a phase transition to change to ice.
57. The method of claim 46, wherein the step of preparing a sample comprises a step of spatially separating the analytes within the medium by electrophoresis.
58. The method of claim 57, wherein the step of irradiating the frozen sample comprises a step of irradiating sequentially a plurality of positions within the frozen sample, wherein at least two irradiated positions correspond to locations of the spatially separated analytes.
59. The method of claim 58, wherein each of the plurality of positions is irradiated by radiation delivered in pulses, each pulse having a duration of less than the relaxation time of a selected vibrational mode of at least one component of the medium, wherein the pulses are separated in time by intervals, each interval having a duration of at least ten times the relaxation time of the selected vibrational mode.
60. The method of claim 58, wherein each of the plurality of positions is irradiated by radiation delivered in pulses, each pulse having a duration of less than a thermal

relaxation time of the at least one component of the medium.

61. The method of claim 58, wherein each of the plurality of positions is irradiated by radiation delivered in pulses, each pulse having a duration of less than a mechanical relaxation time of the at least one component of the medium.
62. The method of claim 46, wherein the medium includes an electrophoresis medium.
63. The method of claim 62, wherein the electrophoresis medium comprises polyacrylamide.
64. The method of claim 46, further comprising the steps of:
  - a. passing the ionized analytes through a mass spectrometer; and
  - b. obtaining a mass spectrum of the ionized analytes.
65. A system for desorption and ionization of analytes, comprising:
  - a. means for preparing a sample having analytes in a medium including at least one component;
  - b. means for freezing the sample at a sufficiently low temperature so that at least part of the sample has an increase in viscosity and a decrease in vapor pressure; and
  - c. means for irradiating the frozen sample with short-pulse radiation to cause medium ablation and desorption and ionization of the analytes.
66. The system of claim 65, further comprising:
  - a. means for selecting a resonant vibrational mode of at least one component of the medium; and
  - b. means for selecting an energy source tuned to emit short-pulse radiation substantially at the wavelength of the selected resonant

vibrational mode.

67. The system of claim 66, wherein the energy source is a laser.
68. The system of claim 67, wherein the laser is a free electron laser.
69. The system of claim 68, wherein the free electron laser is tunable to generate short-pulse radiation.
70. The system of claim 67, wherein the laser is a solid state laser.
71. The system of claim 70, wherein the solid state laser is tunable to generate short-pulse radiation.
72. The system of claim 66, wherein means for selecting a resonant vibrational mode comprises means for locating the resonant vibrational mode from a Fourier-transform infrared absorption spectrum of the medium.
73. The system of claim 65, wherein the freezing means includes a sample support to contain the sample, and the sample support being immersed in liquid nitrogen for a period of time so that any water within the sample has a phase transition to change to ice.
74. The system of claim 65, wherein the medium includes an electrophoresis medium.
75. The system of claim 74, wherein the electrophoresis medium comprises polyacrylamide.
76. The system of claim 65, further comprising means for obtaining a mass spectrum of

the ionized analytes.

77. A system for desorption and ionization of analytes, comprising:
- a. a support for holding a sample of analytes in a medium;
  - b. a laser source emitting light corresponding to a selected vibrational mode of at least one component of the medium;
  - c. optics elements directing the emitted light to irradiate the sample to cause medium ablation and desorption and ionization of the analytes;
  - d. an ion accelerator for injecting the ionized analytes into a mass spectrometer;
  - e. a mass spectrometer that separates the accelerated ionized analytes according to their masses;
  - f. a detector for the mass determination of ionized analytes separated according to their masses;
  - g. data collection equipment for recording of the spectrum of determined masses; and
  - h. data presentation equipment for displaying of the spectrum of determined masses.
78. The system of claim 77, wherein the laser source emits light in pulses, each pulse having a duration of less than 5.0 picoseconds, wherein the pulses are separated in time by more than 100 picoseconds.
79. The system of claim 77, wherein the support for holding a sample of analytes includes means for moving the sample in a relative motion back and forth to the laser light to form a rastering trace such that the desorption and ionization of the analytes occur substantially at a same region in space.
80. The system of claim 79, wherein the detector and data collection equipment are in

communication with the irradiating means such that the spectrum of determined masses at each position is separately recorded.